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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| EXAMINER | |
|---|---|
| HINES, JANA A | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1645 | |

DATE MAILED: 11/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/656,055 | YAVER ET AL. | |
| | Examiner | Art Unit | |
| | Ja-Na Hines | 1645 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *06 September 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,11,27,34,36,42,43 and 80-93* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,11,27,34,36,42,43 and 80-93* is/are rejected.

7)☒ Claim(s) *27* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Amendment Entry*

1. The amendment filed on September 6, 2006 has been entered. Claims 1, 36 and 42 have been amended. New claims 80-93 have been added. Claims 2-10, 12-26, 28-33, 35, 37-41 and 44-79 have been cancelled. Claims 1, 11, 27, 34, 36, 42-43 and 80-93 are under consideration in this office action.

### *Withdrawal of Rejections*

2. The following rejections have been withdrawn in view of applicants' amendments and arguments:

a) The rejection of claims 1, 11, 27, 34, 36, 42 and 43 under 35 U.S.C. 112, first paragraph;

b) The rejection of claims 1, 11 and 27 under 35 U.S.C. 102(b) as being anticipated by Zhang et al; and

c) The rejection of claims 1, 11, 34, 36 and 42-43 under 35 U.S.C. 102(b) as being anticipated by Wilson et al.

### *Response to Arguments*

3. Applicant's arguments filed September 6, 2006 have been fully considered but they are not persuasive.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. The rejection of claims 1, 11, 27, 34, 36, 42 and 43 under 35 U.S.C. 112, second paragraph, is maintained for reasons already of record.

a) Applicants' assert that the terms "subinhibitory amount" and "similarity or dissimilarity" have been defined on pages 11-12 and 22-23. The specification states that the subinhibitory amount is based on the MIC of the antimicrobial compound against a bacterium and cultivation of the bacterium. There is no definition of an actual amount. One of ordinary skill in the art would only be reasonably apprised that the subinhibitory amount is based on the MIC of the antimicrobial compound against a bacterium. The definition is relative term, thus the term is indefinite.

Pages 22-23 do not state a standard for determining similarity or dissimilarity. Pages 22-23 discuss looking at expression profiles and determining similarity or dissimilarity. However the specification does not address the metes and bounds of what is similar or dissimilar and there is no criteria which defines how to determine whether something is similar or not. Thus the rejection is maintained and applicants' arguments are not persuasive.

b) Applicants' urge that page 23 which states that hybridization complexes are significantly different from the nucleic acid sample will provide a signature expression profile. However there is no teaching of what types of detected levels of expression are deemed significantly different and what levels are not different. The specification does not disclose any criteria to determine these differences. Thus the term is not defined by the claim, the specification does not provide a standard for ascertaining the requisite

degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Thus the claim is unclear and appropriate clarification is required to overcome the rejection. Therefore the rejection is maintained and applicants' arguments are not persuasive.

### *New Grounds of Objection and Rejection*

### *Claim Objections*

5. Claim 27 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The dependant claim is not further limiting because the independent claim already requires that the plurality of sequence be obtained from *B. subtilis*. Therefore appropriate clarification is required to overcome the rejection.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 80-93 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to

one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Neither the specification nor originally presented claims provides support for the method of determination wherein the plurality of sequences correspond to less than about 75%, 50%, 25%, 10%, 5%, or 2% of the genome of the *B. subtilis* cells. The specification nor originally presented claims provides support for the method of determination method wherein the difference in the detected expression level is about 10% to 100% or greater.

Applicant did not point to support in the specification for a method wherein the plurality of sequences correspond to a percentage of the genome of the *B. subtilis* cells or wherein the difference in the detected expression level is about 10% to 100% or greater. Moreover, applicant failed to specifically point to the identity of the newly claimed method steps. Therefore it appears that the entire specification appears to fail to recite support for the newly recited method steps. At best pages 21-22 discuss data analysis, however the computational methods are used for the interpretation of microarray based expression profiles with include cluster analysis. The instantly recited claims are not drawn to microarray based expression profiles with include cluster analysis. Furthermore the instantly claimed methods do not require evaluating the results of the microarray statistical analysis to determine the significant of the differences in expression levels. Therefore, the claims incorporate new matter. Accordingly, it appears that there is no support in the specification. Therefore, applicants must specifically point to page and line number support for the identity of the

method as recited by the newly added claims. Therefore, the new claims incorporate new matter and are accordingly rejected.

***Claim Rejections - 35 USC § 101***

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

7. Claims 80-81 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The instant claims are drawn to a method of determination comprising subject the values to a program for analysis wherein the program comprises a computer algorithm.

Claims to computer-related inventions that are clearly nonstatutory are not patentable. In this context, "functional descriptive material" consists of data structures and computer programs which impart functionality when employed as a computer component. (The definition of "data structure" is "a physical or logical relationship among data elements, designed to support specific data manipulation functions." The New IEEE Standard Dictionary of Electrical and Electronics Terms 308 (5th ed. 1993).) Such types of descriptive material are nonstatutory when claimed as descriptive material per se. *Warmerdam*, 33 F.3d at 1360, 31 USPQ2d at 1759.

In the instant case, the claims are drawn to a program for analysis wherein the program comprises a computer algorithm. Moreover, the instant claims are not drawn to functionally descriptive material recorded on some computer-readable medium, nor does the program have any actual components thereby making the program structurally

and functionally interrelated to the method. The instant claims are to a computer algorithm that does nothing more than solve mathematical problems or manipulate abstract ideas or concepts. Thus, a process consisting solely of mathematical operations, i.e., converting one set of numbers into another set of numbers, does not manipulate appropriate subject matter and thus cannot constitute a statutory process. In practical terms, claims define nonstatutory processes if they: consist solely of mathematical operations without some claimed practical application i.e., executing a "mathematical algorithm" See *Schrader*, 22 F.3d at 294-95, 30 USPQ2d at 1458-59. Therefore the claims are rejected.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 1, 11, 27, 34, 36 and 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhang et al., in view of Kunst et al.

The claims are drawn to a method for determining the mode of action of an antimicrobial compound, comprising: a) detecting hybridization complexes formed by contacting at least one nucleic acid sample, obtained by culturing *Bacillus subtilis* cells in the presence of at least one subinhibitory amount of an antimicrobial compound having an unknown mode of action, with a plurality of nucleic acid sequence

corresponding to genes of the *Bacillus subtilis* cells, wherein the presence, absence or change in the amount of the hybridization complexes detected, compared with hybridization complexes formed between the plurality of nucleic acid sequences and a second nucleic acid sample obtained from the *Bacillus subtilis* cells cultured in the absence or presence of a standard compound having a known mode action, is indicative of the similarity or dissimilarity of the mode of actions of the antimicrobial compound and the standard compound; and b) assigning a mode of action for the antimicrobial compound based on the similarity or dissimilarity of values assigned to the hybridization complexes detected in (a) based on the hybridization complexes formed from the second nucleic acid sample. The dependant claims are drawn to action of the antimicrobial compound and the source of the plurality of nucleic acids.

Zhang et al., teach regulated gene expression in *Staphylococcus au*reus for identifying antibiotic mode of action. The selective modulation of gene expression levels is a very powerful strategy and allows for the gaining of valuable information (page 297). Regulated gene expression is useful for studying gene function and evaluating molecular targets for antibiotic discovery (page 297). Well-regulated gene control systems have been use of *Escherichia coli* and *Bacillus subtilis* (page 297). Thus, the authors demonstrate that the sequences can be obtained from *Bacillus subtilis,* just as required by the claims. Zhang et al., demonstrates how modulating target expression levels is linked to the antibacterial activity of selected compounds with their proposed cellular target (page 298). Section 3.3 teaches the examination of antibiotic mode of action (page 302). The authors identified an actininin-like compound

which inhibits protein synthesis in bacteria by preventing the removal of the N-formyl group from newly synthesized polypeptides (page 302-3). Thus the antibacterial compound is a member of the class of compounds which inhibit protein synthesis, just as required by the claims. The compound was contained in media which also comprised the bacterial cells (page 304). Thus, Zhang et al., teach that the bacterial cells were cultured in the presence of at least one subinhibitory amount of an antimicrobial compound having an unknown mode of action just as required by the claims. Zhang et al., teach hybridization techniques via PCR and Western blotting as a means for assessing gene expression (page 304). The PCR techniques teach the hybridization of at least one nucleic acid hybridizing to the nucleic acids within the plurality of nucleic acid sequences. The hybridization complexes were detected by western blotting teachings, just as required by the claims. Therefore the art teaches hybridization as the means for analyzing gene expression just as the claims require. The results compare the unknown compound against another well-known antibiotic, mupirocin, which acts as the standard. See also Table 1 (page 304). Therefore Zhang et al., teach culturing and detection of hybridized complexes in the absence or presence of a known of standard compound having a known mode of action just as required by the claim. The comparison allows for the authors to conclude that the antibacterial activity of the compound appears to be due to its inhibition of the target enzyme (page 304). Thus, the art teaches that the comparison between the unknown and known modes of action are indicative or similarities or dissimilarities of the modes of action of between the two, just as required by the claims. However Zhang et al., do not use the *Bacillus subtilis* cells.

Kunst et al., teach the that nucleic acids can be the genes and fragments of *Bacillus subtilis.* Kunst et al., describe that complete genomic sequence of *Bacillus subtilis.*

Therefore, it would have been prima facie obvious at the time of applicants invention to exchange the gram-positive bacteria as taught by Zhang et al., used within the method for determining the mode of action of an antimicrobial compound, comprising a detection of hybridization complexes, a comparison of the hybridization complexes to a standard compound having a known mode action, and assigning a mode of action for the unknown antimicrobial compound based on the similarity or dissimilarity of values assigned to the hybridization complexes detected from the known sample for the gram-positive *Bacillus subtilis* bacteria as taught by Kunst et al. No more than routine skill would have been required to exchange an equivalent and functionally alternative gram-positive bacteria for another for use in a method of determination. Thus one would have a reasonable expectation of success since the prior art already teaches that *Bacillus subtilis* is an ideal regulated gene expression system.

***Conclusion***

9. No claims allowed.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 571-272-0859. The examiner can normally be reached on Monday-Thursday and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Bruce Campell, can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ja-Na Hines
October 24, 2006

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